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ACRYLIC INVESTMENT OF INTRACRANIAL ANEURYSMS

BY

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My original intimation of this subject was presented to give preliminary notification of a new method of treating bleeding intracranial aneurysms (Dutton, 1956), unsuitable for clipping or ligation, and previously considered manageable only by the uncertain method of muscle wrapping. Logue (1956) comments thus: "... surrounding the sac wall with a coat of hammered muscle to support it from the outside, a procedure which surely must have more effect on the surgeon's peace of mind than on the aneurysm." He also notes in 9% of his cases "contraindications to surgery" due to "anomalies of the anterior part of the circle of Willis, so that both anterior cerebral arteries arise from one internal carotid trunk, with the result that occlusion of the anterior cerebral is not feasible." Hook and Norlén (1958) wrapped 8 out of an operative series of 57 middle cerebral aneurysms.

The passage of time has allowed of the addition of further cases for study, and this paper contains an appraisal of this method consequent on a three-year follow-up. Certain additional advantages are also discussed, especially in relation to accidental rupture during surgical operation. Details of experimental work and aseptic techniques are also presented.

Experimental Work

The method was originally developed to provide an immediate unyielding investment for the sac and parent vessels. "Simplex rapid" cold curing acrylic made by Dental Fillings Limited was finally selected, because its physical properties were most suitable, and though certain drawbacks were known (Lefkowitz *et al.*, 1949; Zander, 1951; Kramer and McLean, 1952; Coy *et al.*, 1952; van Huysen and Boyd, 1953; Müller and Maeglin, 1953; Massler and Silberkweit, 1954; Nygaard-Östby, 1955; Kramer, 1955, 1956), relating to the use of "self-curing" acrylics in experimental dental caries, its use was thought to be practicable. This material was known to withstand immersion in saline fluids for long periods, to set with a smooth surface, to show minimal shrinkage only during polymerization

of the order of 6% by volume, corresponding to approximately 2.7% linear, and investigations on heat production revealed that small quantities—that is, 1–2 ml.—when allowed to polymerize, reached 115° F. (46.1° C.). With intracranial use such temperature production was thought to be of small moment, especially in the presence of cerebrospinal fluid and saline wash. The problem of incomplete polymerization, amounting to between 1% and 5%, was also considered to be amenable to the same method of dissipation.

In vivo experiments were then conducted, goats being found entirely suitable. Initially, collars of acrylic were made around peripheral limb vessels, and the immediate, early, and late results noted. There were no immediate effects on the vessel or limb circulation, no infection or foreign-body reaction, the collar was well accepted by the host; and, most important, there was no encystment, the collar being firmly felted. Segments of the vessel and collar were studied, and histologically the intima was found to be healthy, the media was normal, and fibrosis of the adventitia was found to be not great. There was no sign whatsoever of thrombus deposition in the vessel.

Acrylic and bone-wax (as control) implants and vessel investments were then made into the cerebral sulci of goats, to study the immediate and delayed vascular and cellular effects. Specimens were examined at varying post-implant periods ranging from seven days to seven weeks. Two blocks of cortex removed after seven days were frozen and stained for nerve-cell bodies (carbol azure) and for lipoid (scharlach R and haematoxylin). In a few sections from one block a narrow wedge-shaped zone of increased cellularity was seen around one of the small cortical vessels, which passed through the nerve-cell layer into the subcortical white matter. No other sign of damage to the brain underlying the implanted material (acrylic) was found. In a control block from the same animal in which bone wax had been inserted a similar zone of perivascular reaction was seen. Here the course of the vessel was similarly marked out by macrophage cells containing granules of neutral fat.

Blocks of cortex removed seven weeks later were also examined. In all, the molecular layer of the cortex showed increased cellularity (Figs. 1 and 2) below the site of insertion. In this situation a mild proliferation of astrocytes had occurred accompanied by an increase in the number of microglial cells, the processes of which were often slightly swollen and could be visualized in ordinary nerve-cell preparations. At one point the superficial part of the grey matter showed a slight increase in microglial cells, but nowhere had there been any detectable destruction of neurones. The microglial cells did not contain lipoid.

Summarizing, one can say that the insertion of acrylic had produced a mild localized microglial and astrocytic reaction in the molecular layer of the cortex, but its presence had not proved detrimental in any way to the underlying nerve cells. The narrow wedge-shaped areas of perivascular damage are to be regarded as the consequence of the surgical procedure and cannot be directly related to the effect of the acrylic, since similar appearances were seen in the control sections.

Bacteriology, with Special Reference to Cobalt Irradiation

The powder (polymer) as received from the manufacturers is probably sterile; all tested specimens have failed to produce any organisms, but contamination is easily effected, and the addition of monomer to effect

polymerization is no guarantee that sterility will be preserved. The monomer certainly exerts some bacteriostatic influence on bacteria, but it does not destroy them. The polymerized acrylic is porous, and infected material has the ability to contaminate tissues. When staphylococci of a known strain were added to monomer, polymer, or polymerizing paste and then moulded into a cuff around a rolled tube of sterile filter paper, culture of the latter in broth revealed a heavy growth. Robinson and Macalister (1954) reproduced these findings in animal experiments.

Originally, autoclaving of the powder was advocated, but experience soon proved that any period in excess of five minutes proportionately destroyed the benzoyl peroxide and polymerization was then delayed. Autoclaving for 20 minutes caused the reaction to be delayed as long as 24 hours. An alternative method of sterilization was thus required, and one which would not interfere with the activator systems or adversely affect the physical properties. I am indebted to Dr. Tudway, of Bristol General Hospital, for the treatment of the polymer with 2 to 3 million rads by means of cobalt radiation. The powder was placed in a special "perspex" container and submitted to radiation from radioactive cobalt during two successive nights, from

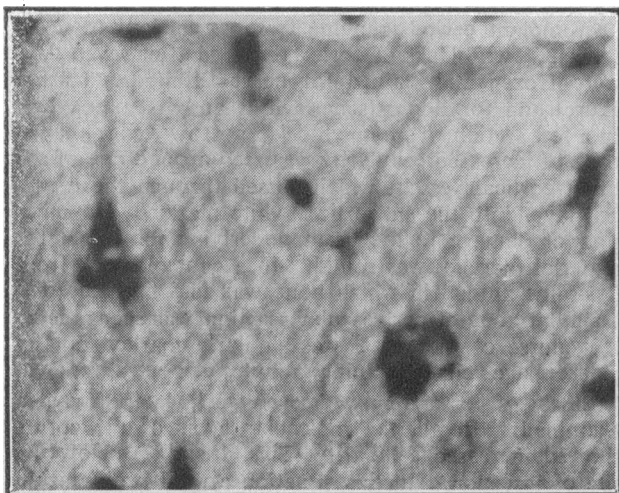


FIG. 1.—Normal appearance. Molecular layer from cortex remote from operation site, normal cell density. (Carbol azure. $\times 360$.)

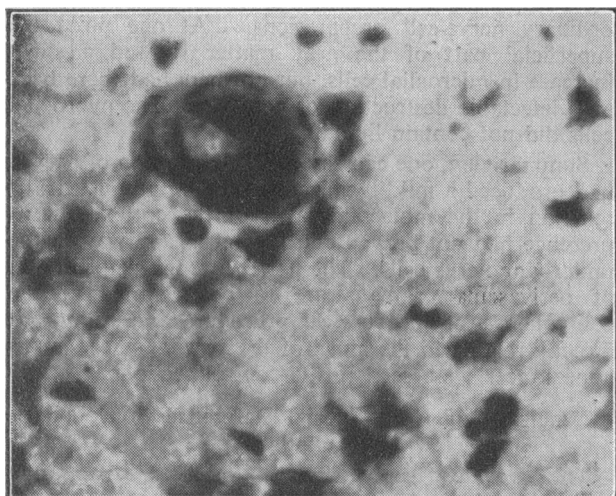


FIG. 2.—High-power view of the proliferated astrocytes and microglial cells of the affected molecular layer. (Carbol azure. $\times 240$.) (Preparation by Dr. R. M. Norman.)

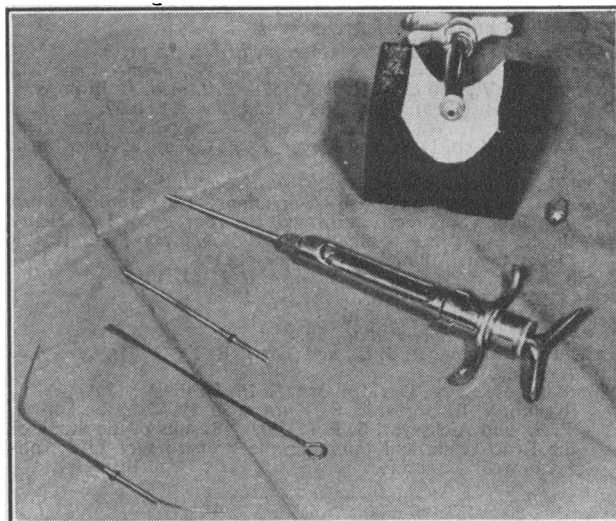


FIG. 3.—Dental syringe modified with a large drill-hole so that a large-bore needle can be introduced, the distal end being blunt. The curved needle may also be of value in getting into difficult areas.

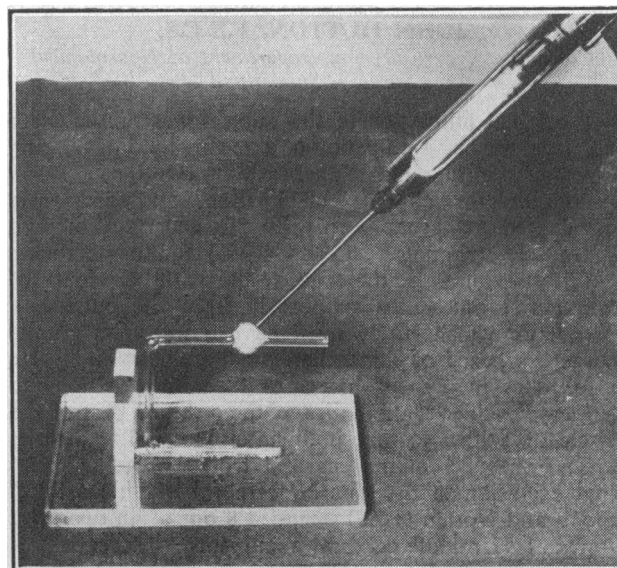


FIG. 4.—After vigorously shaking the cartridge the material slowly gels in three minutes, and during this time it is suitable for injection through the cannula. The illustration shows a model aneurysm being invested.

5 p.m. till 9 a.m. Previous heavy contamination with organisms including sporebearers was completely destroyed. Control non-irradiated specimens gave heavy growths. Polymerization was completely unaffected. Sterilization of the monomer was easily effected by means of a pressure Seitz filter, and it was then sealed in sterile ampoules.

The Method

Sterile polymer is put up into sterile empty dental anaesthetic cartridges. The monomer is introduced by needle puncture of the cap of the cartridge, a proportion of three of polymer to one of monomer being roughly correct. Vigorous shaking promotes an even mix, and when the consistency is that of thick cream it is ready for application. About three minutes is required to this stage—the material quickly becomes too thick to pass the wide-bore cannula—and polymerization is "completed" in about a further five minutes, the material being quite firm. At the thick-cream stage it

flows around the vessel and sac, forming a collar, and can be moulded by means of a gutta-percha "sling" (Figs. 3 and 4).

Review of Cases

All the cases were of subarachnoid haemorrhage requiring surgical intervention in which the angiographic investigation suggested the impossibility or technical difficulty of ligation or clipping, either proximal or of the neck of the aneurysm (Fig. 5). Carotid ligation in the neck was thought to be suitable only in certain cases of aneurysm at the posterior communicating artery level or lower, and was never practised for aneurysms of the middle cerebral or anterior cerebral. All cases were

artery, which was supplied by a "right-sided" anterior cerebral artery taking origin from the left internal carotid. No anterior cerebral branch was evident arising from the right internal carotid, and there was no vessel representing the anterior cerebral on the left side proximal to the anterior communicating. The anatomy was thus complex, and proximal or local clipping was inapplicable. The chiasm was screened with a small sheet of gutta-percha and acrylic investment performed. Polymerization was "complete" in eight minutes, the complex sac and entrant vessels all being covered. There was no alteration in vessel calibre or brain circulation.

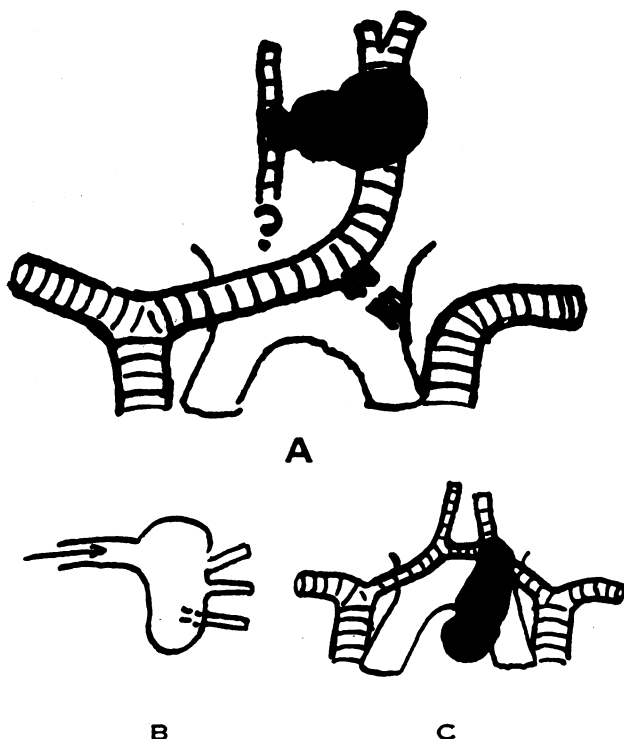


FIG. 5.—A, Anterior communicating aneurysm; abnormal vascular pattern. B, Middle cerebral aneurysm. C, Anterior cerebral aneurysm.

operated upon under general anaesthesia, respiration control being used and hypothermia being artificially induced to an average of 29.5° C. On certain occasions hypotension was artificially induced. All cases were anaesthetized by Dr. P. L. F. Mortimer, and his contribution to their success is noted and appreciated.

Whenever conventional methods of treatment were more appropriate they were invariably used, and thus in three years only 17 cases are available for study. They comprise nine cases of the anterior communicating artery and eight of the middle cerebral artery.

Aneurysms of the Anterior Communicating Artery (Nine Cases)

Case 1

A man aged 36 had his initial subarachnoid haemorrhage five weeks before admission and his second haemorrhage two weeks before. Within three days of admission he was submitted to operation, after angiograms had displayed a multilobular aneurysm of the anterior communicating artery, filling from the left anterior cerebral artery only, and with considerable spasm of the internal carotid artery proximal to its termination. At operation on January 23, 1956, the aneurysm was seen to comprise a bilobed anterior and unilobar posterior sac about the anterior communicating

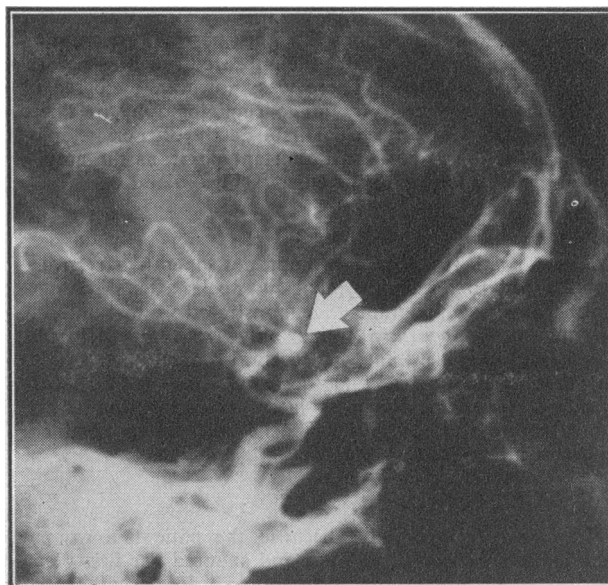


FIG. 6.—Case 1. Pre-operative left carotid arteriogram. Siphon shows slight narrowing of its calibre; a berry-shaped aneurysm is shown on the anterior cerebral artery in the midline, close to the site of origin of anterior communicating artery or possibly arising from the latter. Both anterior cerebrals fill only from the left and are centrally placed.

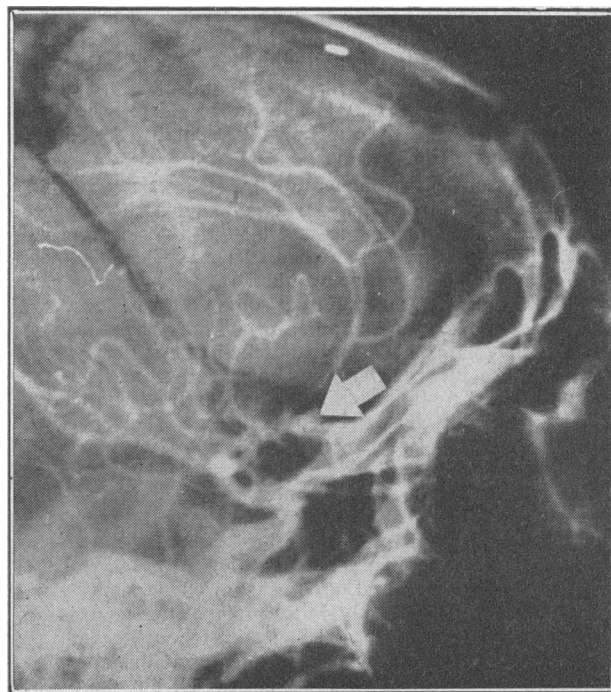


FIG. 7.—Case 1, after investment. Post-operative left carotid arteriogram. Compared with the previous series, the siphon and neighbouring vessels are now of normal calibre. The aneurysm is only slightly smaller. Note evidence of ventricular dilatation.

The patient, pre-operatively, was somnolent, showing signs and symptoms of raised intracranial pressure, appearing ill, with an ominous dusky suffusion. He was well immediately after the procedure, but in a few days became increasingly somnolent, apathetic, and incontinent. Then after a few more days began a slow and gradual return to superficial normality one month later, though he was somewhat disorientated and, for a period, showed a minor euphoric apathy with some impairment of normal social responsibility. One year later he was almost back to his normal (pre-haemorrhage) state. His Dundee accent was again noticeable, and he volunteered that his working capacity was about 75% of normal. He had then been back to his normal occupation as a fitter for five months. Three weeks after operation angiograms demonstrated no spasm or interruption of the vessels, the aneurysmal sac appeared much as before, though it was smaller. There was, however, a degree of hydrocephalus, revealed by air encephalography. There was no evidence of any visual field defect on perimeter or screen to white and red—an important point, as the acrylic material had lain close to the chiasm (Figs. 6 and 7).

Case 2

A man aged 31 made a prompt post-operative recovery and returned to his employment six weeks after discharge. Pre-operative angiograms demonstrated an anterior communicating aneurysm filling only from the left side, there being no evident anterior cerebral branch on the right. His first haemorrhage had occurred one week before operation, his second four days later. On admission he had a most severe and ominous headache and was in imminent danger of a third haemorrhage.

Case 3

This case was instructive because the patient, a woman aged 34, was 24 weeks pregnant and suffered her first bleed one and a half weeks prior to operation. Both mother and foetus tolerated without incident hypothermia of 30.6° C. for several hours and surgical intervention. At the beginning of the operation the spasm seen in the angiograms was noted. During dissection of the sac the fundus ruptured and haemostasis was secured by means of a Norlén clip across the body of the sac; and the clip, the sac, and entrant vessels were then all invested with acrylic. The patient was discharged back to her original hospital after one week, and later gave birth to a normal child at full term. Parturition was complicated by haemorrhage requiring transfusion, and three and a half months later she died suddenly from acute liver atrophy, presumably secondary to homologous serum jaundice.

Examination of the specimen revealed an invested aneurysm with no sign of further haemorrhage, though there was a defect in the shell of acrylic where both anterior cerebral arteries distal to the sac emerged. The orifice for these vessels was larger than one would have wished, and it is possible that haemorrhage could at some time have occurred from this site. The sac and anterior communicating arteries were free from thrombus, and the shell of the acrylic was felt in place by a thin fibrous capsule derived from the arachnoid and was stained with haemosiderin. The inferomedial border of the right frontal lobe showed some absorption of the grey matter with two tiny areas of absorption in the underlying white matter immediately adjacent to the acrylic shell. Otherwise the brain appeared quite normal, showing no signs of infarction in the distribution of either anterior cerebral artery or elsewhere, and these findings were confirmed histologically. One of the emerging anterior cerebral arteries showed a patchy subintimal fibrosis, severe only in one place, the companion vessel being otherwise normal. It was thought that this subintimal proliferation was a little greater at this site than one would expect to see in a woman of 34, but there was also a great deal of thickening and change within the internal carotid artery on the left side, considerably proximal to the scene of operation or haemorrhage. No direct inferences

can therefore be made from these findings save to note that the presence of the acrylic, after being in place for nine and a half months, had resulted in no gross alteration in the normal appearances of the vessels.

Cases 4-9

Four further cases progressed satisfactorily, but the next two patients subsequently died after operation, neither death being attributable apparently to the method of treatment.

Case 8.—A man aged 40 suffered his first haemorrhage three weeks and the second one three days before operation. He was somnolent, with raised intracranial pressure and a left hemiparesis prior to operation. Angiograms revealed a left anterior cerebral artery only, with considerable spasm of the internal carotid vessel and anterior cerebral on that side and a sac lying at the level of the anterior communicating artery. He progressed satisfactorily for two days post-operatively and then developed a right-sided weakness and became unresponsive. A second operation was performed, but nothing abnormal was noted apart from considerable enlargement of the gyri. He died shortly afterwards, and examination of the specimen revealed that massive cerebral oedema of uncertain origin was the cause of his demise. The sac and parent vessels were satisfactorily encased in the acrylic and there was no thrombosis.

Case 9.—A man of 55 developed a weakness of all his limbs excepting the left arm after an apparently successful operation, and died a month later, mainly from severe disturbances of metabolism with gross fluctuations of electrolyte values. At necropsy there was no thrombosis, and no evident haemorrhage from the sac since operation. It was presumed that his signs and progress post-operatively were the result of spasm or delayed thrombosis of the perforated vessels, though no marked softening could be detected.

Aneurysms of the Middle Cerebral Artery (8 Patients)

In all patients the presenting findings pre-operatively were minimal weakness and, in appropriate cases, dysphasia. All but one had bled twice, the weakness or dysphasia invariably following the second haemorrhage, for which they were referred to the neurosurgical unit. Their ages varied from 35 to 55 years, and in all cases angiograms demonstrated spasm either proximal or immediately distal to the sac. All operations were conducted under hypothermia; and initially, as a first step, a silk thread was placed around the middle cerebral artery proximal to the immediate operation area. In each case the sac was either giving origin to a primary branch vessel or was so involved that clipping the neck was inadvisable or the neck was difficult to define clearly without causing a rupture.

All patients recovered, the motor weakness clearing up quickly; the speech defects were usually much later in clearing. Two patients showed prompt improvement of their speech defect immediately after recovery from the anaesthetic, and it was presumed that this was due to an immediate improvement in the circulation (Figs. 8 and 9). Pre- and post-operative electroencephalograms and angiograms suggested no disturbance to the circulation and function of the middle cerebral territory.

Recurrent Haemorrhage

To date there has been no proved case of recurrent haemorrhage in any of the survivors, and review of the necropsy reports in the two cases of aneurysm of the anterior communicating artery showed no evidence of recurrent haemorrhage. One case of the anterior communicating group required re-exploration

and frontal lobectomy because of a haemorrhagic, swollen, and necrotic area in the brain substance. This was not a case of expansion of the depths of the sulci with clot, and there was no evident communication with the aneurysmal sac. The age of the blood clot was considerable, and it was not known whether this clot had originated before the first operation or occurred subsequently.

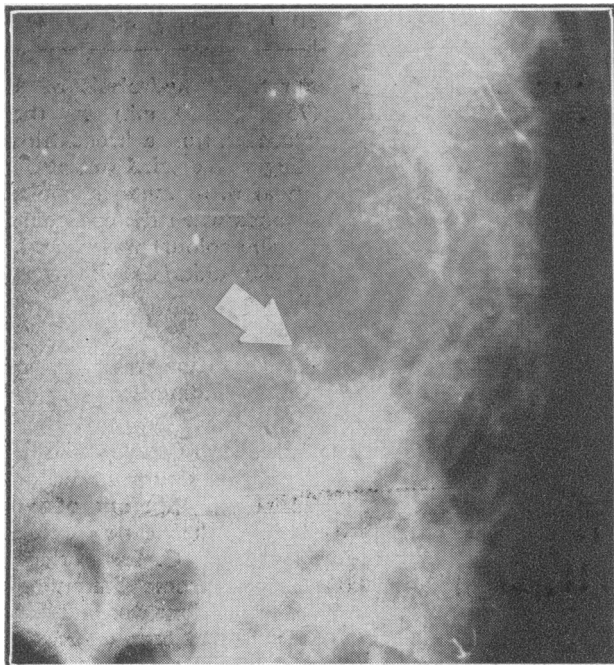


FIG. 8.—Pre-operative left carotid arteriogram. A berry aneurysm is shown lying on the middle cerebral artery, about 1.8 cm. from its origin; the fundus is directed upwards and is lying proximal to any primary branch of the main stem.

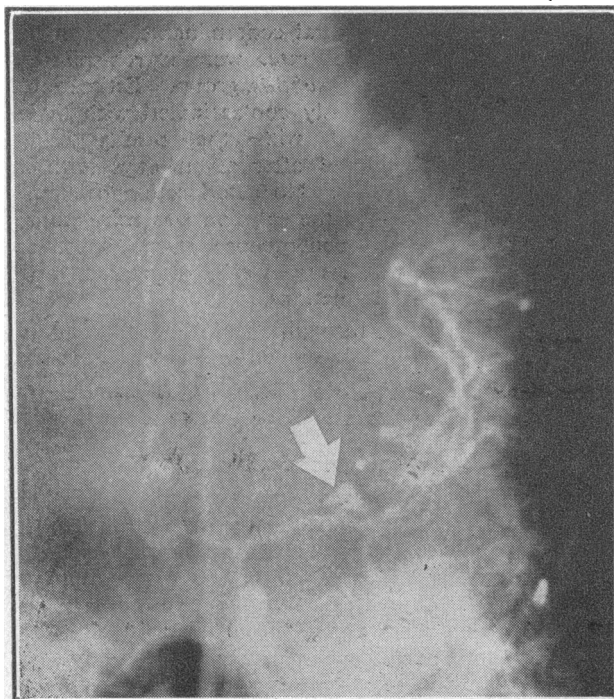


FIG. 9.—Same case as Fig. 8, after investment. Post-operative left carotid arteriogram. This is comparable with the pre-operative findings. The shift as shown on the antero-posterior view was the result of cerebral oedema and subdural hydroma which subsequently resolved.

Certain Special Points of Technique

A clear definition of the sac is required for this method to be effective. This may be a tedious procedure, and sometimes it is profitable to suck away the adjacent brain, especially if necrotic or softened with clot (Norlén and Olivecrona, 1953). The sac can be further prepared for investment by passing a thread behind the parent vessel, so that gentle traction can elevate the sac from its "bed." This allows the semi-fluid acrylic to flow around to the deep surface and cover all parts of the sac. Sometimes assistance is given by a thread clipped to neighbouring arachnoid with a silver clip. Frequently a sheet of gutta-percha placed beneath the sac has acted as an efficient hammock to aid in moulding the acrylic, especially in relation to the optic chiasma and basal cisterns. Should one be unable to remove the stamp after polymerization is "complete," the excess can be trimmed away and no harm ensues from the retained fragment. On all occasions the optic chiasma has been screened and no visual field defects have been noted.

Premature rupture has been treated by means of a clip applied at any convenient distance from the neck of the sac (if possible) to secure haemostasis. The sac remnant, clip, and parent vessel can then be invested. This method can be adapted to treat large aneurysmal sacs. Middle cerebral aneurysmal ruptures have also been dealt with fairly easily by means of a temporary proximal ligature (thread) on the middle cerebral artery, a hammered muscle graft applied, and the whole then invested.

Conclusion

This method would appear to be safe and effective, and should be accepted as a recognized means of treating aneurysmal sacs not suitable for other methods. Personal communications indicate that this method has now been tried in different clinics throughout the world and without any apparent drawbacks (af Björkstén and Troupp, 1958).

Experimental work has established its acceptance and tolerance by the body and freedom from sepsis. A follow-up of the patients during a three-year period indicates its effectiveness. On certain occasions, especially cases of accidental rupture, it has definite advantages, and has proved of great value in difficult situations. Furthermore, experience has shown that its use has not been associated with the spasm of local arteries which can so disastrously affect the outcome of a potentially successful case after ligation.

Summary

Acrylic investment has been found satisfactory in experimental work and in a three-year follow-up of patients.

Seventeen cases with subarachnoid haemorrhage have been treated—nine due to aneurysms of the anterior communicating artery and eight affecting the middle cerebral artery.

The middle cerebral group did uniformly well. Two of the anterior communicating series died after operation from causes not directly attributable to the method.

The technique is simple and asepsis is easily achieved.

Certain advantages of the method have become apparent with experience.

It is a pleasure to record my indebtedness to my neuro-surgical preceptor, Mr. George Alexander, and to my

colleagues at the South-western Regional Neurosurgical Unit, Mr. Douglas Phillips and Mr. Allan Hulme, who encouraged me to make use of the method in their cases and for allowing me access to their notes, and to specially thank Mr. G. F. Rowbotham, of the Regional Centre of Neurological Surgery, Newcastle upon Tyne, who also referred three cases to me. I am especially grateful to Dr. R. M. Norman and Dr. R. Sandry, of the Neuro-pathological Laboratory, Frenchay Hospital, Bristol, for the histological studies. I also wish to acknowledge the grant made by the University of Bristol Department of Surgery and to Professor Masservy and staff of the Veterinary College, Langford, for facilities for the preliminary experimental work.

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SERUM AMYLASE ESTIMATIONS IN DIFFERENTIAL DIAGNOSIS

BY

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"The diastase content of each individual is very constant, so that deviations from this normal value are significant" (Somogyi, 1938, 1941). The simplest laboratory investigation used in differentiating acute pancreatitis from other "acute abdomens" is the serum amylase estimation. Occasional rises encountered in other abdominal emergencies (Burnet and Ness, 1955), after the administration of opiates (Wapshaw, 1953), in mumps (Wolman *et al.*, 1947), after alcohol (Carter, 1945), in renal failure and other miscellaneous conditions (Polowe, 1946), have thrown doubt on its value. This study is a critical evaluation of a rapid "side-room" serum amylase estimation in conditions which often present as a differential diagnosis of acute pancreatitis. In addition, the case histories of those conditions other than acute pancreatitis where a rise was encountered have been analysed to try to demonstrate any common factors.

For the purposes of this study serum amylase estimations were carried out on 454 patients, divided as follows: (a) 45 cases of pancreatitis (41 acute and 4 chronic) in which the diagnosis was made in 32 cases on clinical grounds in conjunction with a raised serum amylase, in 11 cases by laparotomy, and 2 cases at necropsy (Table II); (b) 337 cases of conditions recorded as the differential diagnosis of acute pancreatitis; and (c) 72 miscellaneous causes of acute abdominal pain.

Method.—The method used was a modification of Somogyi's iodometric technique as described by King

TABLE I.—Serum Amylase Estimations in 454 Cases

Diagnosis	Serum Amylase (Units/100 ml.)				Total No. Cases
	< 200	200–355	400–640	800+	
Acute appendicitis ..	85	5	Nil	Nil	90
Exacerbation of peptic ulcer ..	81	6	"	"	87
Perforated viscus ..	20	12	2	1	35
Intestinal obstruction ..	29	5	Nil	Nil	34
Coronary thrombosis ..	30	Nil	"	"	30
Acute cholecystitis ..	55	5	"	1	61
Miscellaneous ..	67	4	"	1	72
Acute pancreatitis ..	Nil	2	12	27	41
Chronic pancreatitis ..	2	1	1	Nil	4

(1946). This measures the rate of hydrolysis of a standard starch solution (75 mg./100 ml.) by the amylase at 37° C. to erythrodextrin, achrodextrin, maltose, and glucose. Sampling was carried out at 30 seconds and one minute, then at two-minute intervals, reverting to intervals of 30 seconds when the end-point (a final disappearance of any blue colour) was neared. A normal range of 60 to 200 units/100 ml. was established.

Precautions

(a) Blood for serum amylase estimation was taken in all cases prior to operation or administration of morphine derivatives.

(b) McGeachin (1953) stated that no deterioration in serum amylase activity occurred in serum stored at 4° C. for periods up to 72 hours. Six out of 30 consecutive serum amylases of the early cases, redetermined after refrigeration at 4° C. for periods varying from 12 to 24 hours, showed some diminution in activity. In consequence, all estimations were carried out immediately the blood samples had been taken.

(c) Salivary contamination of the starch substrate was prevented by incorporating cotton-wool filters in all pipettes.

(d) Amylase-producing organisms may be introduced into the substrate and cause deterioration. The commonest significant natural contaminants, shown by daily cultures of the substrate, were starch-splitting organisms of the *Bacillus subtilis* group. Estimations using starch solution grossly contaminated with these cultures were compared with the results using uncontaminated starch and after seven days with a freshly prepared substrate. No deterioration occurred over this period provided the solution was refrigerated when not in use. In consequence starch substrate was prepared freshly every week, stoppered, and refrigerated between estimations.

(e) The difficulty of recognition of the end-point in artificial light or with bile-stained serum was obviated by the use of a white tile, on to which equal volumes of the sample and iodine were placed.

Acute Pancreatitis

The ranges of serum amylase encountered in the 41 cases of acute pancreatitis can be seen in Table I. Twenty-four were 1,100 units or above, and all determined within 24 hours of the onset of symptoms were 533 units or greater. A pre-operative diagnosis of acute pancreatitis was made only once without the aid of enzyme studies, and here laparotomy had to be resorted to for confirmation (Case 35, Table II). Four of the 15 other cases proved by laparotomy (Cases 3, 5, 19, and 57) died post-operatively, whereas only 2 of the 25 with a raised serum amylase treated conservatively were fatal.